AMENDMENTS TO THE SPECIFICATION:

Amend the specification as follows.

After the title insert the following new paragraph:

The present application is a divisional of U.S. Application Serial No. 09/898,461, filed July 5, 2001, the entire contents of which is hereby incorporated by reference.

Page 4, delete the paragraph spanning lines 15-24 and insert the following therefor:

In a first aspect, the invention provides a CPG2 enzyme in which an immunogenic region selected from:

KIKGRGGK (amino acids 98-105, SEQ ID NO:1)

KEYGVRD (157-163, SEQ ID NO:2), preferably YGVRD (159-163 (SEQ ID NO:6))

KLADY (191-195, SEQ ID NO:3)

GAGK (412-C-terminal(415), SEQ ID NO:4),
preferably AG (413-414),

EGGKKLVDK (331-338, SEQ ID NO:5)

is modified to reduce or alter immunogenicity to a mammalian immune system whilst retaining CPG2 activity.

Page 5, delete the paragraph on line 25 and insert the following therefor:

Figure 3B shows the amino acid sequence of CPG2 (SEQ ID NO:7).

Page 9, delete the paragraph spanning lines 11-18 and insert the following therefor:

The MFE-23::CPG2-his fusion protein has a hexa-His tag at the C-terminus of CPG2. This tag may be extended by inserting sequences of varying length between the

hexa-His tag and the C-terminus of CPG2. Insertions include the myc tag (EQKLISEEDLN (SEQ ID NO:8)) to result in a myc-his tag having the sequence AAASFLEQKLISEEDLNSAVDHHHHHH (SEQ ID NO:9), or a humanized version of the myc tag. Such insertions may serve to mask immunogenic surfaces on the CPG2 protein.

Page 11, delete the paragraph spanning lines 4-33 and insert the following therefor:

Replacement of these immunogenic regions may be by human sequences of similar sequence to the wild type sequence, or by sequences exhibiting similar conformations, or by sequences exhibiting similar hydrophobic, charge, stereochemical or surface exposure characteristics. In an example procedure, the sequence, conformation and interior protein contact profile of an immunogenic region would be encoded as a set of criteria on which to search and select similar regions from a database of human protein three-dimensional structures (for example, the protein databank (PDB) could be searched using the IDITIS software (Oxford Molecular plc, UK)). Such selected regions would then be ranked on their similarity to the above criteria and the most similar sequence or sequences used for replacement of an existing immunogenic region. Where the humanised sequences comprise the same or similar residues involved in internal packing interactions as the wild type sequence, the humanised sequence may not require further modification. If, however, these residues result in structural perturbations of the internal interactions with the rest of the molecule, these buried residues may be substituted with residues present in the wild-type molecule, producing a hybrid sequence which retains internal packing interactions and stereochemistry. Examples of suitable regions found using this method for replacement of the KEYGVRD sequence (SEQ ID NO:2) include the hybrid sequence (maintaining intramolecular contacts) YEYGVMK (SEQ ID NO:10) of the humanised sequence YEVGMMK (SEQ ID NO:11). Examples of suitable sequences for replacement of

KLADY (SEQ ID NO:3) include the hybrid sequence (maintaining intramolecular contacts) RNSDY (SEQ ID NO:12) of the humanised sequence RNSDR (SEQ ID NO:13).

In a related aspect of the invention, we have found that

Page 31, delete the paragraphs spanning lines 1-22 and insert the following therefor:

Table 1. CPG2 variants tested for CM79 binding and enzyme activity. A single mutation was made in each variant (bold) in either the KEYGVRD (SEQ ID NO:2) or the GAGK (SEQ ID NO:4) regions. Wild-type MFE-23::CPG2 and variant V6 were CEA affinity chromotography and FPLC purified for CM79 binding, serum binding and enzyme activity assays.

Insert the attached Sequence Listing after the Figures.